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Long-term follow-up in optimally treated and stable heart failure patients: primary care vs. heart failure clinic. Results of the COACH-2 study

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Aims It has been suggested that home-based heart failure (HF) management in primary care may be an alternative to clinic-based management in HF patients. However, little is known about adherence to HF guidelines and adherence to the medication regimen in these home-based programmes. The aim of the current study was to determine whether long-term follow-up and treatment in primary care is equally effective as follow-up at a specialized HF clinic in terms of guideline adherence and patient adherence, in HF patients initially managed and up-titrated to optimal treatment at a specialized HF clinic.

Methods and results We conducted a multicentre, randomized, controlled study in 189 HF patients (62% male, age 72 ± 11 years), who were assigned to follow-up either in primary care ($n = 97$) or in a HF clinic ($n = 92$). After 12 months, no differences between guideline adherence, as estimated by the Guideline Adherence Indicator (GAI-3), and patient adherence, in terms of the medication possession ratio (MPR), were found between treatment groups. There was no difference in the number of deaths ($n = 12$ in primary care and $n = 8$ in the HF clinic; $P = 0.48$), and hospital readmissions for cardiovascular (CV) reasons were also similar. The total number of unplanned non-CV hospital readmissions, however, tended to be higher in the primary care group ($n = 22$) than in the HF clinic group ($n = 10$; $P = 0.05$).

Conclusions Patients discharged after initial management in a specialized HF clinic can be discharged to primary care for long-term follow-up with regard to maintaining guideline adherence and patient adherence. However, the complexity of the HF syndrome and its associated co-morbidities requires continuous monitoring. Close collaboration between healthcare providers will be crucial in order to provide HF patients with optimal, integrated care.

Keywords Heart failure • Primary care • Disease management • Adherence

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Introduction

Although treatment of heart failure (HF) has improved in the past decades with the development of multiple medications and devices, mortality and morbidity are still considerable.[1,2] In addition to optimal medical management, the HF guidelines[3] recommend enrolling HF patients in a multidisciplinary care management including follow-up after discharge (by visits, telephone support, or remote monitoring). An important issue is whether long-term management of HF patients must remain under the care of a HF clinic (in a hospital), or whether patients can be referred back to their general practitioner (GP) to be further managed in the primary care setting. There is little documentation and limited evidence suggesting that follow-up in primary care ensures successful continuation of evidence-based therapy. Moreover, the study of Ojeda and colleagues[4] showed that after ending an intervention programme, the results of the initial optimization and education decreased within the next year.[4] Clearly, if such a home-based programme in primary care were to be similarly effective, this would have great clinical, practical, and economic advantages. However, the optimal model for the delivery of long-term multidisciplinary care management is still unknown.[5,6]

Recent large-scale studies show that not all models are equally successful in improving outcomes and they indicate that a tailored approach to HF management is needed.[7,8]

The WHICH? trial which was conducted in Australia indicated that a home-based HF management programme was equally effective in terms of outcome and was associated with lower healthcare costs compared with an equivalent clinic-based programme.[9] In the much larger Danish NorthStar study, it was shown that stable HF patients on optimal therapy did not benefit from long-term follow-up in a specialized HF clinic, and, indeed, they could be referred back safely to their GP.[10]

Although these studies reported baseline medication, they did not examine whether guideline-recommended HF medication was continued throughout the study. This is important since it has been shown that guideline adherence in HF patients primarily treated by their GP is lower than in patients treated by cardiologists, which may at least be partly attributable to the fact that GPs usually deal with older patients with more co-morbidity.[11–13] GPs seem to experience barriers in the initiation and optimization of pharmacological treatment.[14] Little is known about the long-term adherence to HF guidelines after initial optimization of medication. Patient compliance, nowadays knows as patient adherence, is an important predictor of outcome in HF,[15,16] and patients often have difficulty in remaining compliant with treatment in the long run.[4] The role of patient adherence to guideline therapy in home-based management programmes has not been studied yet.

We therefore designed the Comparative study On guideline Adherence and patient Compliance in Heart failure patients (COACH-2) study.[17] The COACH-2 study aimed to determine whether long-term follow-up in primary care can be equally effective as follow-up in a specialized HF clinic in terms of adherence to the guideline-recommended HF medication and patient adherence to medication with these recommendations.

Methods

Study design

The COACH-2 study was a multicentre, non-inferiority, randomized, controlled trial, and a detailed description of its rationale and design has been published previously.[17] The COACH-2 trial was approved by the Central Ethics Committee of the University Hospital Groningen and performed according to the Declaration of Helsinki. The study is listed in the Netherlands Trial Register (NTR1729).

Study patients

Patients were recruited from four outpatient HF clinics in The Netherlands. HF clinics were all sited in hospitals delivering specialized consultative healthcare, in a department with personnel and facilities for advanced medical investigation and treatment. All visiting patients were screened for their eligibility to participate in the study. Patients were eligible if they: (i) had documented symptoms of HF (either currently or at the time of diagnosis); (ii) had HF with evidence for structural underlying ventricular dysfunction (LVEF <45% at the time of diagnosis); (iii) were up-titrated to optimal pharmacological treatment [ACE inhibitors/ARBs, beta-blockers, and mineralocorticoid (aldosterone) receptor antagonists (MRAs)] for NYHA III patients according the European Society of Cardiology (ESC) guidelines of 2008;[18] (iv) clinically stable for at least 1 month, i.e. no hospital admission in the previous month, no visits to the emergency unit for decompensated HF in the previous month, and no unplanned medication changes in the previous month; (v) optimally educated and informed about HF and the required lifestyle changes; and (vi) 18 years or older.

Exclusion criteria included (i) management by a cardiologist planned for diagnostics or, if additional treatment was needed, according to the cardiologist or GP; (ii) the GP had substantial arguments against patient participation in the study; (iii) the patient was unable to fill in data collection materials; (iv) the patient had a life expectancy <6 months; (v) the patient was living in a nursing home; or (vi) the patient had a current psychiatric disorder.

Study procedure

Patients and their caregivers were informed about the study when visiting the outpatient HF clinic in one of the participating centres. Thereafter, patients were titrated to optimal, guideline-recommended HF medication and were educated about HF, its treatment, and lifestyle changes. After being titrated to optimal HF medication and confirmed stable for at least 4 weeks, patients were approached to participate in the study and to give their informed consent. Patients were then randomly allocated to follow-up by their GP (PC group) or follow-up by the HF clinic (HF clinic group). GPs were randomly selected following the randomization of patients and were not specifically trained for this study. Contacts and visits in both groups were assumed to take place according to the European guidelines for treatment of acute and chronic heart failure[18] and according to the Dutch Multidisciplinary Guideline on Chronic Heart Failure.[19] Within the HF clinic group, contact with the GP was possible following the 'care as usual' principle. Within the PC group, no visits at the HF clinic were scheduled; however, consultation of the HF clinic by the GP was possible. At the end of the follow-up period (12 months), all patients from both treatment groups were invited to an end of study visit at the HF clinic.

Study outcomes

This study had two primary outcomes, guideline adherence and patient adherence. It was hypothesized that long-term follow-up under the described conditions would be equally effective in both groups in terms of guideline adherence and patient compliance at 1 year follow-up. Guideline adherence was measured by means of the Guideline Adherence Indicator (GAI) [20], including guideline-recommended prescription of an ACE inhibitor (or ARB) and a beta-blocker for all patients, and spironolactone in patients with NYHA ≥ III. Guideline adherence for the primary endpoint was defined as a GAI of 100%. The other primary endpoint was patient adherence with medication in terms of the medication possession ratio (MPR) calculated from digital pharmacy records over 12 months of follow-up. The MPR reflects the number of days for which the prescribed medication was available for patients based on their drug refill behaviour following the prescribed medications.[21]

Medication that started after randomization was not included, unless it was a switch between drugs within the same therapeutic class. Patients who died during follow up ($n = 20$) and patients who had their drugs weekly delivered automatically by a multidose medication dispenser system ($n = 31$) were excluded from the analyses. For 17 patients, pharmacy data were missing or incomplete. Secondary outcomes included mortality and readmission rates. The researchers adjudicated hospital readmissions based on the medical records and blinded for group assignment.

Statistical analysis

The trial was powered for a non-inferiority comparison for guideline adherence. Non-inferiority for guideline adherence was considered proven if the lower limit of the one-sided 95% confidence interval (CI) of the difference between adherence during the GP follow-up and the HF clinic follow-up did not exceed a margin of 20%. In total, 75 patients randomized to receive standard care and 75 patients to receive primary care are needed to demonstrate non-inferiority assuming a standard care guideline adherence rate of 60% and a power of 80%.

Categorical variables, including the primary endpoint, were compared with the χ^2 test or Fisher's exact test, where appropriate. Continuous data were presented as the mean ± SD or median plus interquartile range (IQR), depending on the distribution of the data. Mann–Whitney U-tests were used for comparison of non-normally distributed continuous data and Student' *t*-test for normally distributed continuous data. The analysis of the secondary primary endpoint, patient adherence, was performed by using the Mann–Whitney U-test for non-normally distributed percentages or MPRs. Incidence rates and incidence rate differences per year were determined for death and readmissions per treatment group. A *P*-value of <0.05 was considered statistically significant.

Statistical analyses were performed using SPSS version 12.0 (Chicago, IL, USA) and STATA version 12.1 (College Station, TX, USA) on an intention-to-treat basis.

Results

Patients

A total of 419 patients met the inclusion criteria (*Figure 1*). Of these, 230 were not willing to participate for various reasons such as 'not willing to be referred to their GP' ($n = 160$), 'not willing to visit the HF clinic' ($n = 12$), 'participation too stressful' ($n = 34$), 'refusal to participate in research studies' ($n = 21$), and other reasons ($n = 3$). The remaining 189 patients were the present study population, and they were randomized to either follow-up in primary care ($n = 97$) or follow-up at the HF clinic ($n = 92$).

The mean age of the patients was 72 ± 11 years, and they were predominantly male (62%) and were mainly classified as NYHA II or III at baseline. Co-morbidities such as diabetes, COPD, and AF were common, and there were no significant differences in baseline characteristics between the groups (*Table 1*).

Primary endpoints

Guideline adherence

Since titration to optimal, guideline-recommended medication was an inclusion criterion, guideline adherence at baseline was high, with 90% and 87% in the PC and HF clinic group, respectively. Guideline-recommended medication rates were high, with 90% and 92% of patients having an ACE inhibitor or ARB prescribed in the PC and HF clinic group, respectively.

Primary care, as compared with follow-up at the HF clinic, resulted in similar rates of guideline adherence at 12 months follow-up (81% and 80%, respectively; difference, 1.0%; 95% CI −10 to 12%; *P* for non-inferiority <0.001). In total, 94% and 90% of patients had a beta-blocker prescribed in the PC and HF clinic group, respectively, and 43% and 53% of patients had an MRA prescribed in the PC and HF clinic group, respectively. Prescription rates at 12 months follow-up were similar to baseline rates (*Table 2*)

Guideline adherence, as estimated by the GAI-3, did not show significant differences between both treatment groups at baseline or at 12 months follow-up (*Tables 2* and *3*).

Patient adherence

The MPR was calculated per therapeutic class (ACE inhibitor/ARB, beta-blocker, and MRA) using a fixed 1-year period (365 days) following the date of randomization. Analysis of patient adherence data is based on 120 patients (*Table 4*). Patients who died during follow-up ($n = 20$) and patients who had their drugs delivered weekly automatically by a multidose medication dispenser system ($n = 31$) were excluded from these analyses. For 18 patients, pharmacy data were missing or incomplete. During follow-up, no significant differences between patients in the PC group and patients in the HF clinic group were found for any of the medication classes or for the average total score. Patient adherence in terms of the MPR was high for both ACE inhibitor/ARB (93.5% and 95.2% in the PC group and HF clinic group, respectively) and beta-blockers (93.5% and 94.9% in the PC group and HF clinic group, respectively). Patient adherence for MRA was 87.1% in the PC group and 93.3% in the HF clinic group.

Secondary outcomes

During the 12 months follow-up period, 20 patients died, 12 (12%) in the PC group and 8 (9%) in the HF clinic group ($P = 0.48$). In total, 42 patients had an unplanned rehospitalization within 12

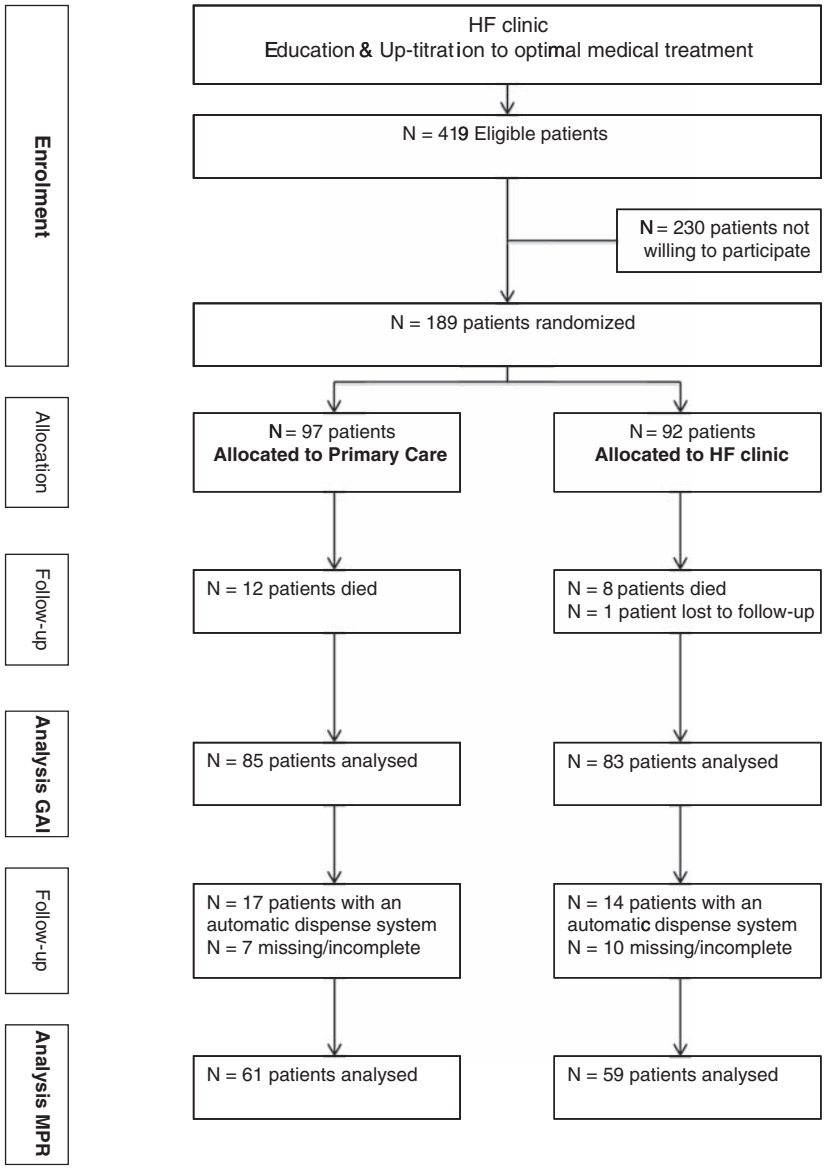

Figure 1 Flow diagram: screening, randomization, follow-up, and analyses. GAI, Guideline Adherence Indicator; HF, heart failure; MPR, medication possession ratio.

months, 25 patients in the PC group and 17 patients in the HF clinic, resulting in a total of 58 unplanned hospital readmissions, with 13 patients being hospitalized more than once (*Table 5*). Readmissions for HF and other cardiovascular (CV) reasons were similar in both treatment groups (8 vs. 7 for HF and 5 vs. 6 CV reasons in the PC group vs. the HF clinic group, respectively).

The number of unplanned non-CV hospital readmissions tended to be higher in the PC group, with 22 vs. 10 readmissions in the HF clinic group ($P = 0.05$). Some patients had more than one non-CV readmission, and the difference in number of patients readmitted between both groups was not significant ($P = 0.09$). Reasons for these non-CV hospital readmissions in both treatment groups are presented in *Table 6*.

Discussion

The COACH-2 study compared guideline adherence and patient adherence in two different HF care delivery models, i.e. home-based management by the GP in primary care vs. hospital-based management in a HF clinic, in patients initially managed and up-titrated to optimal treatment at the specialized HF clinic. The main finding of the study is that after initial uptake and optimization of HF treatment in a specialized HF clinic, long-term follow-up by GPs in primary care is similar, i.e. non-inferior in terms of guideline adherence and adherence to medication in patients. During follow-up, the number of deaths as well as the number of hospitalizations for CV reasons were similar between groups, while the

Table 1 Baseline characteristics per treatment group

	Primary care ($n = 97$)	HF clinic ($n = 92$)
Demographics		
Age	73 ± 10	72 ± 12
Gender (female)	36 (37%)	36 (39%)
Medical history		
Myocardial infarction	43 (44%)	35 (38%)
Diabetes (type I and II)	28 (29%)	15 (16%)
COPD	18 (19%)	17 (18%)
History of atrial fibrillation	45 (46%)	33 (36%)
Admission in past 6 months	10 (10%)	7 (8%)
Heart failure/clinical		
NYHA class		
NYHA I	12 (12%)	7 (8%)
NYHA II	75 (77%)	69 (75%)
NYHA III	10 (10%)	16 (17%)
NYHA IV	–	–
Blood pressure (mmHg)		
Systolic	119 ± 16	120 ± 20
Diastolic	69 ± 9	71 ± 11
Heart rate (b.p.m.)	69(16/44–150)	71 (11/44–100)
LVEF (%/SD)		
At diagnosis	32 ± 9	31 ± 9
Most recent	40 ± 11	37 ± 11
Aetiology		
Ischaemic	47 (48%)	43 (47%)
Duration of HF (days)	1134 (1312)	1095 (938)
≤2 years	51 (53%)	46 (50%)
>2 years	46 (47%)	46 (50%)
Laboratory (median or mean ± SD)		
NT-proBNP (ng/L), median (Q1–Q3)	1115 (410–1771); ($n = 77$)	825 (360–2142); ($n = 69$)
Sodium (mmol/L)	140 ± 2.7	139 ± 5.7
Potassium (mmol/L)	4.3 ± 0.5	4.4 ± 0.4
Creatinine (μmol/L)	110 ± 32	108 ± 37
GFR (mL/min/1.73 m^2)	57 ± 18; $n = 64$	58 ± 19; $n = 63$
Medication class adherence		
ACE inhibitor or ARB	88 (91%)	85 (92%)
Beta-blocker	91 (94%)	83 (90%)
MRA	42 (43%)	49 (53%)
Other cardiac medication		
Diuretics	79 (81%)	79 (86%)
Thiazide	5 (5%)	3 (3%)
Digoxin	14 (14%)	14 (15%)
Statins/lipid-lowering agents	54 (56%)	50 (54%)
Nitrates	15 (15%)	17 (19%)
Anticoagulants	54 (56%)	54 (59%)

Values are given as the mean ± SD or *n* (%).
GFR, glomerular filtration rate; HF, heart failure; MRA, mineralocorticoid receptor antagonist.

Table 2 Medication class adherence at baseline and 12 months

	Primary care		HF clinic	
	Baseline ($n = 97$)	Follow-up ($n = 85$)	Baseline ($n = 92$)	Follow-up ($n = 83$)
ACE inhibitor/ ARB	88 (91%)	77 (91%)	85 (92%)	74 (90%)
Beta-blocker	91 (94%)	79 (93%)	83 (90%)	76 (93%)
MRA	42 (43%)	41 (48%)	49 (53%)	44 (54%)

HF, heart failure; MRA, mineralocorticoid receptor antagonist.

Table 3 Guideline Adherence Indicator-3 total scores at baseline and 12 months per treatment group

	Primary care % (95% CI)	HF clinic % (95% CI)	*P*-value
GAI-3 total baseline[a]	95.0 (91.8–98.2)	94.6 (91.0–98.1)	0.85
GAI-3 total 12 months[a]	91.6 (87.7–95.4)	91.1 (86.9–95.3)	0.87
Difference	−3.4 (−5.6 to −1.3)	−3.4 (−6.0 to −0.90)	0.99

CI, confidence interval; GAI-3, Guideline Adherence Indicator.
[a]Mineralocorticoid receptor antagonist corrected for NYHA class.

Table 4 Patient compliance in medication possession ratio per medication class at 12 months

	Primary care	HF clinic	Difference
ACE inhibitor/ARB	93.5% ($n = 51$)	95.2% ($n = 53$)	0.67
Beta-blocker	93.5% ($n = 57$)	94.9% ($n = 56$)	0.42
MRA	87.1% ($n = 23$)	93.3% ($n = 26$)	0.28
Average total score	92.3% ($n = 61$)	94.4% ($n = 59$)	0.10

HF, heart failure; MRA, mineralocorticoid receptor antagonist.

number of non-CV hospitalizations tended to be higher ($P = 0.05$) in the PC group.

The present findings are in line with the results of the NorthStar study,[10] which showed that clinically stable HF patients on optimal medical therapy can be safely referred back to follow-up in primary care in terms of mortality and HF readmissions. The current study provides additional evidence in that long-term follow-up at a HF clinic does not lead to a benefit in terms of guideline adherence and patient adherence in clinically stable patients with mild to moderate HF.

Despite optimal treatment and presumed clinical stability, 20 out of 189 patients died within a year and 58 unplanned hospital admissions occurred. More than half (55%) of these hospitalizations were for non-CV reasons, which is in line with the results of the first COACH study.[7] Importantly, we observed more

Table 5 Numbers and incidence rates of death and readmissions per treatment group

	Primary care ($n = 97$)	IR/year	HF clinic ($n = 92$)	IR/year	IR difference (95% CI)
Total no. of deaths	12	0.128	8	0.092	−0.036 (−0.133 to 0.061); $P = 0.481$
Cause of death					
Stroke	1		1		
HF	2		2		
Other CV disorders	0		1		
Other non-CV disorders	6		1		
Unknown	3		3		
Total no. of readmissions for HF	8	0.082	7	0.076	−0.006 (−0.086 to 0.073); $P = 0.882$
Total no. of readmissions for CV reasons	5	0.052	6	0.065	−0.014 (−0.055 to 0.083); $P = 0.710$
Total no. of readmissions for non-CV reasons	22	0.227	10	0.109	−0.118 (−0.234 to −0.002); $P = 0.05$

CV, cardiovascular; HF, heart failure; IR; incidence rate.

non-CV hospital admissions in the PC group compared with the HF clinic group, although this was of borderline statistical significance. This relatively high number of non-CV hospitalizations confirms the complexity of the HF syndrome, which is associated with a large number of co-morbidities, particularly in the elderly.[22,23] Although non-significant, baseline differences between both treatment groups, e.g. the prevalence of diabetes, may have influenced the difference in non-CV hospitalizations. Along with these multiple co-morbidities, the clinical course of HF patients is often unpredictable, with clinically stable phases interspersed with periods of exacerbation and deterioration, finally ending in a terminal phase.[24] Over time, patients' needs, treatment, and care may become more complex, often requiring regular adjustments. Continuous monitoring of the patients' condition is therefore needed, and intensive collaboration between primary care and specialized HF care will be crucial in these phases to determine how and where best treatment and care can be provided according to the patient's needs. The ultimate goal, as described by the ESC Heart Failure Association,[22] can be described as 'to provide a "seamless" system of care across primary care and hospital care so that management of every patient is optimal, no matter where they begin or continue their health care journey'.

Limitations

There are potential limitations to the present findings. First, the number of patients enrolled is relatively small and was not powered to detect significant differences in terms of mortality or the number of hospitalizations. Secondly, it is important to note that the generalizability of our study results is limited to the specific conditions that were applied within the COACH-2 study. The study included clinically stable patients with systolic dysfunction who were optimally treated and educated at a specialized HF clinic, mainly classified as NYHA class II, who were followed for a period of 12 months. Whether our conclusion is also generalizable to a longer term and to more severe HF patients remains to be established. Furthermore, a substantial number of patients did not want to participate in the study, mainly because of their preference to receive follow-up care at the HF clinic. This finding may have biased our study population towards patients that are willing to be treated in primary care. Interestingly, this phenomenon was also reported by Stewart *et al.*[9] in the WHICH? trial. Since it is acknowledged that patient preferences are vital in delivering optimal healthcare,[25] patient preferences for a specific delivery model of HF care may be an important dilemma in terms of delivering the patient's choice of care on the one hand vs. cost-effectiveness on the other hand. Finally, as far as the applicability of our findings to other countries is concerned, healthcare in The Netherlands is known as a primary care-based system where the GP acts as the gate-keeper for secondary care and where patients can consult their GP with only limited costs involved.[26] This low threshold may generally be advantageous, but it cannot be excluded that some patients in the present study who were in the HF clinic group also consulted their GPs when they felt that was necessary. GPs are well educated, working with high-quality guidelines for many chronic diseases including HF.[19] European practice guidelines are endorsed by the different echelons of healthcare professionals in The Netherlands. These conditions may be different in other countries with other healthcare systems; the results may therefore not be generalized to countries with other healthcare and educational systems.

Conclusion

Patients discharged after initial management, up-titration, and education at a specialized HF clinic can be discharged to primary care for long-term follow-up with regard to maintaining guideline adherence and patient adherence. This study investigated the first step in optimizing the structural involvement of the GP in long-term HF

Table 6 Non-cardiovascular hospital readmissions in the primary care group and in the heart failure clinic group

Reason for readmission (MeDRA code)	Primary care (*n*)	Heart failre clinic (*n*)
Hypoglycaemia	1	–
Hyperglycaemia	1	–
Nausea and vomiting symptoms	3	1
Asthenic conditions	2	1
Electrolyte and fluid balance conditions	1	1
Melaena	3	1
Respiratory tract infections	5	–
Bronchospasm and obstruction (COPD)	1	–
Dyspnoea	1	–
Gastrointestinal therapeutic procedures	–	1
Abdominal and gastrointestinal infections	–	1
Skin lesion excisions	1	–
Rib fracture	–	1
Lower limb fractures and dislocations	1	
Bone-related signs and symptoms	–	1
Infectious arthritis	–	1
Non-site-specific procedural complications	1	–
Inguinal hernia	1	–
Poisoning and toxicity	–	1
Total	22	10

management. The uptake of treatment and up-titration of medication by GPs in primary care could be a next step that needs further research. The complex clinical picture of HF and the high number of associated co-morbidities needs continuous monitoring. Moreover, close collaboration between healthcare professionals will remain crucial to provide HF patients with integrated, optimal HF care that best fits patients in the different phases of their disease trajectory.

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References

1. Chen J, Normand SL, Wang Y, Krumholz HM. National and regional trends in heart failure hospitalization and mortality rates for Medicare Beneficiaries. 1998–2008. *JAMA* 2011;**306**:1669–1678.
2. McAlister FA, Stewart S, Ferrua S, McMurray JJ. Multidisciplinary strategies for the management of heart failure patients at high risk for admission. A systematic review of randomized trials. *J Am Coll Cardiol* 2004;**44**:810–819.
3. McMurray JJ, Adamopoulos S, Anker SD, Auricchio A, Bohm M, Dickstein K, Falk V, Filippatos G, Fonseca C, Gomez-Sanchez MA, Jaarsma T, Kober L, Lip GY, Maggioni AP, Parkhomenko A, Pieske BM, Popescu BA, Ronnevik PK, Rutten FH, Schwitter J, Seferovic 4P, Stepinska J, Trindade PT, Voors AA, Zannad F, Zeiher A, Bax JJ, Baumgartner H, Ceconi C, Dean V, Deaton C, Fagard R, Funck-Brentano C, Hasdai D, Hoes A, Kirchhof P, Knuuti J, Kolh P, McDonagh T, Moulin C, Reiner Z, Sechtem U, Sirnes PA, Tendera M, Torbicki A, Vahanian A, Windecker S, Bonet LA, Avraamides P, Ben Lamin HA, Brignole M, Coca A, Cowburn P, Dargie H, Elliott P, Flachskampf FA, Guida GF, Hardman S, Iung B, Merkely B, Mueller C, Nanas JN, Nielsen OW, Orn S, Parissis JT, Ponikowski P. ESC guidelines for the diagnosis and treatment of acute and chronic heart failure 2012: the Task Force for the Diagnosis and Treatment of Acute and Chronic Heart Failure 2012 of the European Society of Cardiology. Developed in collaboration with the Heart Failure Association (HFA) of the ESC. *Eur J Heart Fail* 2012;**14**:803–869.
4. Ojeda S, Anguita M, Delgado M, Atienza F, Rus C, Granados AL, Ridocci F, Vallés F, Velasco JA. Short- and long-term results of a programme for the prevention of readmissions and mortality in patients with heart failure: are effects maintained after stopping the programme? *Eur J Heart Fail* 2005;**7**:921–926.
5. Stewart S. What is the optimal place for heart failure treatment and care: home or hospital? *Curr Heart Fail Rep* 2013;**10**:227–231.
6. McAlister FA, Bakal JA, Kaul P, Quan H, Blackadar R, Johnstone D, Ezekowitz J. Changes in heart failure outcomes after a province-wide change in health service provision. A natural experiment in Alberta, Canada. *Circ Heart Fail* 2013;**6**:76–82.
7. Jaarsma T, van der Wal MH, Lesman-Leegte I, Luttik ML, Hogenhuis J, Veeger NJ, Sanderman R, Hoes AW, van Gilst WH, Lok DJ, Dunselman PH, Tijssen JG, Hillege HL, van Veldhuisen DJ, Coordinating Study Evaluating Outcomes of Advising and Counseling in Heart Failure (COACH) Investigators. Effect of moderate or intensive disease management program on outcome in patients with heart failure: Coordinating Study Evaluating Outcomes of Advising and Counseling in Heart Failure (COACH). *Arch Intern Med* 2008;**11**:316–324.
8. Powell LH, Calvin JE Jr, Richardson D, Janssen I, Mendes de Leon CF, Flynn KJ, Grady KL, Rucker-Whitaker CS, Eaton C, Avery E, HART Investigators. Self-management counseling in patients with heart failure: the heart failure adherence and retention randomized behavioral trial. *JAMA* 2010;**304**:1331–1338.
9. Stewart S, Carrington MJ, Marwick TH, Davidson PM, MacDonald P, Horowitz JD, Krum H, Newton PJ, Reid C, Chan YK, Scuffham PA. Impact of home versus clinic-based management of chronic heart failure. *J Am Coll Cardiol* 2012;**60**:1239–1248.
10. Schou M, Gustafsson F, Vedebaeck L. Tuxen C, Keller N, Sejr Knudsen A, Espersen G, markenvard J, Egstrup K, Ulriksen H, Hildebrandt PR. Extended heart failure clinic follow-up in low-risk patients: a randomized clinical trial (NorthStar). *Eur Heart J* 2013;**34**:432–442.
11. Cleland JG, Cohen-Solal A, Aguilar JC, Dietz R, Eastaugh J, Follath F, Fremantle N, Gavazzi A, van Gilst WH, Hobbs FD, Korewicki J, Madeira HC, Preda I, Swedberg K, Widimsky J. Management of heart failure in primary care (the IMPROVEMENT of Heart Failure Programme): an international survey. *Lancet* 2002;**360**:1631–1639.
12. Bosch M, Wensing M, Bakx JC, van der Weijden T, Hoes AW, Grol RPTM. Current treatment of chronic heart failure in primary care; still room for improvement. *J Eval Clin Pract* 2010;**16**:644–650.
13. Dahlstrom U, Hakansson J, Swedberg K, Waldenstrom A. Adequacy of diagnosis and treatment of chronic heart failure in primary health care in Sweden. *Eur J Heart Fail* 2009;**11**:92–98.
14. Kasje WN, Denig P, de Graeff PA, Haaijer-Ruskamp FM. Perceived barriers for treatment of chronic heart failure in general practice; are they affecting performance? *BMC Fam Pract* 2005;**6**:19.
15. Wu JR, Lennie TA, Dekker RL, Biddle MJ, Moser DK. Medication adherence, depressive symptoms and cardiac event-free survival in patients with heart failure. *J Card Fail* 2013;**19**:317–324.
16. Riegel B, Knafl GJ. Electronically monitored medication adherence predicts hospitalization in heart failure patients. *Patient Prefer Adherence* 2013;**5**:1–13.

17. Luttik ML, Brons M, Jaarsma T, Hillege HL, Hoes A, de Jong R, Linssen G, Lok DJ, Berger M, van Veldhuisen DJ. Design and methodology of the COACH-2 (Comparative study on guideline adherence and patient compliance in heart failure patients) study: HF clinics versus primary care in stable patients on optimal therapy. *Neth Heart J* 2012;**20**:307–312.
18. Dickstein K, Cohen-Solal A, Filippatos G, McMurray JJ, Ponikowski P, Poole-Wilson PA, Strömberg A, van Veldhuisen DJ, Atar D, Hoes AW, Keren A, Mebazaa A, Nieminen M, Priori SG, Swedberg K. ESC guidelines for the diagnosis and treatment of acute and chronic heart failure 2008: the Task Force for the diagnosis and treatment of acute and chronic heart failure 2008 of the European Society of Cardiology. Developed in collaboration with the Heart Failure Association of the ESC (HFA) and endorsed by the European Society of Intensive Care Medicine (ESICM). *Eur J Heart Fail* 2008;**10**:933–989.
19. NHG standaard Hartfalen; eerste herziening. *Huisarts en Wetenschap* 2009;**48**:64–76.
20. Komajda M, Lapuerta P, Hermans N, Gonzalez-Juanatey JR, van Veldhuisen DJ, Erdmann E, Tavazzi L, Poole-Wilson P, Le Pen C. Adherence to guidelines is a predictor of outcome in chronic heart failure: the MAHLER survey. *Eur Heart J* 2005;**26**:1653–1659.
21. Vink NM, Klungel OH, Stolk RP, Denig P. Comparison of various measures for assessing medication refill adherence using prescription data. *Pharmacoepidemiol Drug Saf* 2009;**18**:159–165.
22. McDonagh TA, Blue L, Clark AL, Dahlström U, Ekman I, Lainscak M, McDonald K, Ryder M, Strömberg A, Jaarsma T. European Society of Cardiology Heart Failure Association. Standards for delivering heart failure care. *Eur J Heart Fail* 2011;**13**:235–241.
23. Van Veldhuisen DJ, Linssen GCM, Jaarsma T, van Gilst WH, Hoes AW, Tijssen JGP, Paulus WJ, Voors AA, Hillege HL. B-type natriuretic peptide and prognosis in heart failure patients with preserved and reduced ejection fraction. *J Am Coll Cardiol* 2013;**61**:1498–1506.
24. Kheirbek RE, Kheirbek RE, Alemi F, Citron BA, Afaq MA, Wu H, Fletcher RD. Trajectory of illness for patients with congestive heart failure. *J Palliat Med* 2013;**16**:478–484.
25. Spertus JA. Evolving applications for patient-centered health status measures. *Circulation* 2008;**118**:2103–2310.
26. Bruggink-Andre de la Porte PW, Lok DJ, van Veldhuisen DJ, van Wijngaarden J, Cornel JH, Zuithoff NP, Badings E, Hoes AW. Added value of a physician-and-nurse-directed heart failure clinic: results from the Deventer–Alkmaar heart failure study. *Heart* 2007;**93**:819–825.